Evaluation of the Chick Embryo as an In Vivo Test System for Radiopharmaceuticals

S. Haller[1], S. Ametamey[2], R. Schibli[1,2], C. Müller[1]

[1]Center for Radiopharmaceutical Sciences ETHZ-PSI-USZ, Paul Scherrer Institute, 5232 Villigen PSI, Switzerland
[2] Department of Chemistry and Applied Biosciences, ETH Zurich, 8093 Zurich, Switzerland

Introduction: The chick embryo and its chorioallantoic membrane (CAM) are widely used in different fields of biomedical research [1]. In radiopharmaceutical sciences it has been reported that this in vivo model presents a suitable test system for studying the distribution, uptake and kinetics of radiotracers by micro-positron emission tomography (PET) as demonstrated for [^{18}F]fluoride [2]. Moreover, it was recently shown that xenografts grown on the CAM can be used to explore the tumor uptake of novel radiotracers by PET imaging [3].
Aims: The aim of this study was to investigate if the chick embryo is a feasible model for evaluating the biodistribution and in vivo stability of radiopharmaceuticals by single photon emission tomography (SPECT) and PET imaging. For this purpose the behavior of various radiopharmaceuticals was compared in the chick embryo and the mouse. Amongst others the renal radiotracer ^{99m}Tc-DMSA, the bone radiotracer ^{99m}Tc-MDP and ^{18}F-fallypride, which targets the dopamine D2 receptor in the brain, were explored in these two species.
Methods: Fertilized chicken eggs were cultivated for 72 h at 37°C before the egg shell was cracked for ex ovo cultivation of the embryos. After 17-19 d ~60 MBq of ^{99m}Tc-DMSA, ~50 MBq of ^{99m}Tc-MDP or ~10 MBq of ^{18}F-fallypride were injected intravenously into a blood vessel of the CAM or intraperitoneally. The chick embryos were euthanized in liquid nitrogen 1.5-5 h p.i. followed by SPECT or PET acquisitions. SPECT and PET scans lasted between 5 and 15 min depending on the amount of radioactivity left in the organism at scan start. All results were compared with those obtained with the same radiotracers in the mouse model.
Results: SPECT/CT images of the chick embryo after the injection of ^{99m}Tc-DMSA clearly showed uptake of radioactivity in the kidneys. ^{99m}Tc-DMSA is known to have the same biodistribution in mice which was confirmed in our current studies. ^{99m}Tc-MDP accumulated in the bones of chick embryos as well as in the skeleton of mice as demonstrated in our SPECT/CT studies. PET scans revealed uptake of radioactivity in the intestine of the chick embryo after the injection of ^{18}F-fallypride. Accumulation of ^{18}F-fallypride in the dopaminergic regions of the chick embryo brain was difficult to determine due to its small size. In the mouse ^{18}F-fallypride accumulated also in the intestine where dopamine receptors are expressed. Moreover, ^{18}F-fallypride bound to the D2 receptors in the mouse brain. Additionally, in both species accumulation of radioactivity was observed in the bones. This indicated in vivo defluorination since free [^{18}F]fluoride is known to be entrapped in the bones as confirmed in our studies for both species.
Conlcusions: In this work we demonstrated that the tested radiopharmaceuticals have comparable in vivo behaviors in chick embryos and mice. Based on this data, we conclude that the chick embryo could be a reliable and cost-effective alternative to the mouse for the first evaluation of novel radiopharmaceuticals. These promising results warrant further investigations using additional radiopharmaceuticals.

Keywords: Chick embryo, PET, SPECT, radiopharmaceutical, in vivo behavior

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